FORM PTO-1390 (Modified) (REV 11-98) U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE

TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371

ATTORNEY'S DOCKET NUMBER	
203970US6PCT	
U.S. APPLICATION NO. (IF KNOWN, SEE 37 CFR)	09/807413

INTERNATIONAL APPLICATION NO.	INTERNATIONAL FILING DATE	PRIORITY DATE CLAIMED
PCT/EP99/02745	23 APRIL 1999	20 OCTOBER 1998

TITLE OF INVENTION

BAG FOR PRESERVING AND TRANSPORTING STERILE PRODUCTS IN POWDER FORM AND FOR FORMING SOLUTIONS OF SAID PRODUCTS IN THE BAG

APPLICANT(S) FOR DO/EO/US

Marco FALCIANI, et al.

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. ☒ This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. ☐ This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3. ☒ This is an express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1).
4. ☒ A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.
5. ☒ A copy of the International Application as filed (35 U.S.C. 371 (c) (2))
   a. ☐ is transmitted herewith (required only if not transmitted by the International Bureau).
   b. ☒ has been transmitted by the International Bureau.
   c. ☐ is not required, as the application was filed in the United States Receiving Office (RO/US).
6. ☐ A translation of the International Application into English (35 U.S.C. 371(c)(2)).
7. ☒ A copy of the International Search Report (PCT/ISA/210).
8. ☒ Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371 (c)(3))
   a. ☐ are transmitted herewith (required only if not transmitted by the International Bureau).
   b. ☐ have been transmitted by the International Bureau.
   c. ☐ have not been made; however, the time limit for making such amendments has NOT expired.
   d. ☒ have not been made and will not be made.
9. ☐ A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).
10. ☒ An oath or declaration of the inventor(s) (35 U.S.C. 371 (c)(4)).
11. ☒ A copy of the International Preliminary Examination Report (PCT/IPEA/409).
12. ☐ A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371 (c)(5)).

Items 13 to 20 below concern document(s) or information included:

13. ☐ An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
14. ☐ An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
15. ☐ A **FIRST** preliminary amendment.
16. ☐ A **SECOND** or **SUBSEQUENT** preliminary amendment.
17. ☐ A substitute specification.
18. ☐ A change of power of attorney and/or address letter.
19. ☐ Certificate of Mailing by Express Mail
20. ☒ Other items or information:

Request for Consideration of Documents Cited in International Search Report
Notice of Priority
PCT/IB/304
PCT/IB/308

U.S. APPLICATION NO. (IF KNOWN, SEE 37 CFR)	INTERNATIONAL APPLICATION NO.	ATTORNEY'S DOCKET NUMBER
09/807413	PCT/EP99/02745	203970US6PCT

21. The following fees are submitted:.		CALCULATIONS PTO USE ONLY
BASIC NATIONAL FEE (37 CFR 1.492 (a) (1) - (5)) :		
☐ Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2) paid to USPTO and International Search Report not prepared by the EPO or JPO	**$1,000.00**	
☒ International preliminary examination fee (37 CFR 1.482) not paid to USPTO but Internation Search Report prepared by the EPO or JPO	**$860.00**	
☐ International preliminary examination fee (37 CFR 1.482) not paid to USPTO but international search fee (37 CFR 1.445(a)(2)) paid to USPTO	**$710.00**	
☐ International preliminary examination fee paid to USPTO (37 CFR 1.482) but all claims did not satisfy provisions of PCT Article 33(1)-(4)	**$690.00**	
☐ International preliminary examination fee paid to USPTO (37 CFR 1.482) and all claims satisfied provisions of PCT Article 33(1)-(4)	**$100.00**	
ENTER APPROPRIATE BASIC FEE AMOUNT =		**$860.00**
Surcharge of **$130.00** for furnishing the oath or declaration later than ☐ 20 ☐ 30 months from the earliest claimed priority date (37 CFR 1.492 (e)).		**$0.00**

CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE		
Total claims	5 - 20 =	0	x $18.00	**$0.00**	
Independent claims	3 - 3 =	0	x $80.00	**$0.00**	
Multiple Dependent Claims **(check if applicable)**.			☐	**$0.00**	
TOTAL OF ABOVE CALCULATIONS =				**$860.00**	
Reduction of 1/2 for filing by small entity, if applicable. Verified Small Entity Statement must also be filed (Note 37 CFR 1.9, 1.27, 1.28) **(check if applicable)**.			☐	**$0.00**	
SUBTOTAL =				**$860.00**	
Processing fee of **$130.00** for furnishing the English translation later than ☐ 20 ☐ 30 months from the earliest claimed priority date (37 CFR 1.492 (f)).			+	**$0.00**	
TOTAL NATIONAL FEE =				**$860.00**	
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31) **(check if applicable).**			☐	**$0.00**	
TOTAL FEES ENCLOSED =				**$860.00**	
				Amount to be: refunded	$
				charged	$

☒ A check in the amount of **$860.00** to cover the above fees is enclosed.

☐ Please charge my Deposit Account No. in the amount of to cover the above fees.
A duplicate copy of this sheet is enclosed.

☒ The Commissioner is hereby authorized to charge any fees which may be required, or credit any overpayment to Deposit Account No. **15-0030** A duplicate copy of this sheet is enclosed.

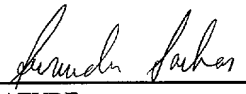
NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO:

22850

(703) 413-3000

Surinder Sachar
Registration No. 34,423



SIGNATURE

Gregory J. Maier

NAME

25,599

REGISTRATION NUMBER

April 19 2001

DATE

BAG FOR PRESERVING AND TRANSPORTING STERILE PRODUCTS IN POWDER FORM AND FOR FORMING SOLUTIONS OF SAID PRODUCTS IN THE BAG

The invention relates to a bag able to preserve a product in powder form under sterile conditions and to enable a liquid to be fed into the bag to form therein a sterile solution ~~//(this term also including a dispersion or suspension)//~~ of said product.

Many products obtained in sterile form in the solid state are known to be used in the liquid state as sterile solutions, suspensions, dispersions or the like.

A typical example is a pharmaceutical product such as an antibiotic or vitamin, or a culture medium for micro-organisms such as cells, bacteria or moulds which at the moment of use is dissolved or dispersed in liquid.

The problem of dissolving or dispersing a sterile powder in liquid while maintaining sterility is considerable and costly, and is solved in various ways, all involving problems which are summarized below by referring to two particularly important cases.

For example, cell culture medium is produced in the form of powder which can be sold as such in polyethylene bags or bottles closed with a screw stopper. To be used, this product is dissolved in liquid to form a solution (typically an amino acid, electrolyte or vitamin solution) in a totally aseptic environment, this involving time and considerable cost.

The sterile solution obtained in this manner is fed into a glass

jar or bottle in a suitable sterile bottling environment, and the sealed bottle is despatched to the client in a special housing and protection container. The user has then to open the bottle under aseptic conditions to be able to then withdraw the solution contained in it.

This method is well known, and is explained for example in lines 9-59 of column 1 of the patent US-A-4,910,147.

To solve these problems, US-A-4,910,147 proposes to sell to the user not the product, but instead an already prepared sterile solution of the cell culture medium enclosed in a sealed flexible bag, into which the solution is fed using semi-automatic aseptic filling machines. Such bags, which are completely filled with the solution, are much more manageable than glass bottles and can be easily and economically despatched by the producer to the user who, without the need for special apparatus or a sterile environment, can directly withdraw all or part of the sterile solution through one or more ports with which the bag is provided.

However, this system also presents problems because although it is relatively simple to store and transport small bags filled with liquid, in the case of bags containing a relatively large liquid volume, for example five litres or more, the hydraulic force exerted by the liquid during transport can break the bag, as is clearly explained in lines 34-50 of column 1 of US-A-4,968,624 ~~6421~~ which names the same inventors and the same proprietor as US-A-4,910,147.

For this reason US-A-4,968,624 describes a very complex rigid structure within which the bags containing the solutions have to be enclosed for their storage and transport.

Again for example, reference can be made to the method of using those sterile crystalline antibiotics (in powder form) contained in single-dose form in glass bottles sealed by rubber plugs. To ~~make~~ ~~user~~ such antibiotics injectable into a patient by using a syringe a sterile solvent (water) is

drawn from a vial (which has firstly to be broken or opened), then the solvent is fed into the bottle by piercing its plug with the syringe needle, the bottle is shaken to dissolve the antibiotic powder, and the solution formed in this manner is drawn into the syringe through the needle which passes through the plug of the bottle, after which the solution can be injected into the patient.

Although this operation may be relatively simple to carry out by a user who has to prepare the solution and inject it only one or a few times a day, it becomes very demanding and costly in hospitals in which specialized personnel (nurses) have to repeat the same operation a very large number of times every day, with considerable time wastage, high cost and serious problems of maintaining sterility, these being enhanced by the need to dispose of a large number of empty glass bottles with rubber plugs, glass vials and miscellaneous packaging material.

Again it should be noted that it is not possible to prepare solutions of antibiotics (for example in bags such as those described in US-A-4,910,147) in suitable plants to then despatch them to hospitals, because such solutions remain unaltered only for a very short time, and then only if special care is taken for their preservation.

In the light of the aforegoing, the main object of this invention is to provide a bag usable for preserving and transporting sterile products in powder form and for feeding into it a solvent to directly form a solution, dispersion or suspension of the powdered product directly within the bag under sterile conditions, the bag being provided with at least one port through which the entire solution or the like or a part thereof can be easily, quickly and safely withdrawn in order to be used.

A further object is to provide a method which enables sterile products in powder form to be packaged in easily storable and transportable flexible bags, and further enables solutions or the like of such products to be subsequently formed directly within

ENCLOSURE 2

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drawn from a vial (which has firstly to be broken or opened), then the solvent is fed into the bottle by piercing its plug with the syringe needle, the bottle is shaken to dissolve the antibiotic powder, and the solution formed in this manner is drawn into the syringe through the needle which passes through the plug of the bottle, after which the solution can be injected into the patient.

Although this operation may be relatively simple to carry out by a user who has to prepare the solution and inject it only one or a few times a day, it becomes very demanding and costly in hospitals in which specialized personnel (nurses) have to repeat the same operation a very large number of times every day, with considerable time wastage, high cost and serious problems of maintaining sterility, these being enhanced by the need to dispose of a large number of empty glass bottles with rubber plugs, glass vials and miscellaneous packaging material.

Again it should be noted that it is not possible to prepare solutions of antibiotics (for example in bags such as those described in US-A-4,910,147 and in US-A-5,364,384) in suitable plants to then despatch them to hospitals, because such solutions remain unaltered only for a very short time, and then only if special care is taken for their preservation.

In order to solve the above mentioned problems the US-A-5,484,431 has proposed the use of a bag constructed from a flexible polyolefin material, sealed at its periphery and defining a closed sterile space containing a sterile solute or a

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soluble product in powder form occupying only a minor portion of the capacity of the bag.

The bag has a plurality of ports through which a liquid can be introduced into it for dissolving the powder or solute and respectively for withdrawing the solution which has been formed within the bag.

According to the teachings of the US-A-5,484,431 the amount of liquid introduced into the bag is such to completely fill it as it is stated, for example, in line 62 of col. 8 and line 23 of col. 9 of the patent specification: in order to make it possible to dissolve the powder or solute contained therein, the bag must include internal means for creating turbulence within its interior (see lines 1-3 of col. 3): preferably the bag is provided with an internal seal 14 (see lines 43-45 and 56-60 of col. 4) which functions to create turbulence when the liquid flows into the bag ensuring an adequate mixing of the liquid and the powder or solute in order to create a solution.

Such solutions are for intravenous administration of dextrose solutions, saline, lactated Ringer's or the like whose concentrations in the respective solutions needs not to be exactly predetermined and the same in each bag.

The structure of the bag disclosed in the US-A-5,484,431 is not a simple one, because it must comprise internal means for creating turbulence within its interior as a consequence of the fact that the liquid introduced therein completely fills the bag, so that a simple shaking of the bag would practically be i AMENDED SHEET completely dissolve

the powder or the solute. Moreover, since the bags are formed with flexible sheet of plastic materials and the bags are completely filled with the liquids introduced therein, it is impossible to obtain solutions all having the same preestablished concentration of the materials dissolved therein.

Finally, the solutions formed in the bags are used for intravenous administration, where it is not necessary to exactly control the amount of the active substances which are administered to the patients.

In the light of the aforegoing, the main object of this invention is to provide a bag of simple structure usable for preserving and transporting sterile products in powder form and for feeding into it a solvent to easily and quickly form a solution with predetermined concentration of the powdered product directly within the bag under sterile conditions, the bag being provided with at least one port through which the entire solution or a part thereof can be easily, quickly and safely withdrawn in order to be used, the volume of the solution being sufficiently large to supply a plurality of single individually usable doses of the same solution, for example for filling a plurality of syringes.

A further object is to provided a method which enables sterile products in powder form to be packaged in easily storable and transportable flexible bags, and further enables solutions with predetermined concentrations of such products to be subsequently easily and quickly formed directly within the bags when is to be used.

These and further objects are attained by a bag for preserving and transporting sterile products in powder form and for forming therein solutions with predetermined concentrations of said products, the bag being of polyolefins construction, being hermetically sealed at its periphery to define a sterile closed space and having at least one port also of polyolefin construction defining a passageway, the two ends of which open inside and respectively outside the bag, said passageway being closed by a pierceable membrane for the introduction of a solvent into the bag and respectively for the withdrawal of the solution therefrom, characterised in that each bag contains an amount of product in powder form adapt to give a solution with desired pre-determined concentration, that such a solution only partially fills the bag capacity, and in that the total amount of said solution is a multiple of single volumes of individual doses of the same solution

The invention concerns also a bag constructed of flexible polyolefin material and containing a ready to use solution prepared by introducing within a sealed bag originally containing a dosed amount of a soluble sterile product in powder form an amount of solvent adapt to give said ready to use solution with desired concentration of said product, characterised in that the bag capacity is such that it is

only partially filled by said ready to use solution, and in that the total volume of said solution is a multiple of single volumes of individual doses of the same solution.

Finally, the invention concerns a method for preparing solutions with predetermined concentrations of soluble sterile products in powder form enclosed and sealed within sterile bags constructed of flexible polyolefin materials, characterised in that a bag containing a dosed amount of soluble sterile product in powder form adapt to give a solution of predetermined concentration is fed with an amount of solvent adapt to give a ready to use solution with desired concentration of the product, in that the bag capacity is such that it is only partially filled by said solution, and in that the volume of the solution suffices to supply a plurality of single individual doses of the same solution.

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The bag structure and its method of use will be more apparent from the ensuing description of a preferred embodiment thereof given by way of non-limiting example with reference to the accompanying drawings, on which:

Figure 1 is a schematic front view of the bag, of which

Figure 2 show an enlarged partial section coplanar with that portion of the bag on which the bag access port is provided;

Figure 3 is a section through the bag taken on the line 3-3 of Figure 1, the bag being shown filled only to a minimum extent with a product in powder form and with the port closed;

Figure 4 is similar to Figure 3, but with the port open for feeding into the bag a liquid having a volume occupying only a part of the bag capacity; and

Figure 5 shows the closed bag inserted into a further two bags used for its storage and its despatch to the powdered product user.

Reference will firstly be made to Figures 1 to 4, which show a bag 1 constructed of polyolefin, preferably low density polyethylene, sealed hermetically along its entire periphery and having at one end a port 2 formed in one piece with and projecting from an elongate tapered body 3 from which there projects a further port

the bags when the solution is to be used.

These and further objects are attained by a bag of polyolefin construction which is hermetically sealed at its periphery and has at least one port also of polyolefin construction defining a passageway the two ends of which open inside and respectively outside the bag, said passageway being closed by a breakable membrane forming part of the port and ensuring the maintaining of sterility within the bag, characterised in that the bag contains a sterile product in powder form, the bag capacity exceeding the directly usable volume of the final sterile product solution, dispersion or suspension obtained by feeding a liquid into the bag through said port and said membrane.

The bag structure and its method of use will be more apparent from the ensuing description of a preferred embodiment thereof given by way of non-limiting example with reference to the accompanying drawings, on which:

Figure 1 is a schematic front view of the bag, of which
Figure 2 shows an enlarged partial section coplanar with that portion of the bag on which the bag access port is provided;
Figure 3 is a section through the bag taken on the line 3-3 of Figure 1, the bag being shown filled only to a minimum extent with a product in powder form and with the port closed;
Figure 4 is similar to Figure 3, but with the port open for feeding into the bag a liquid having a volume occupying only a part of the bag capacity; and
Figure 5 shows the closed bag inserted into a further two bags used for its storage and its despatch to the powdered product user.

Reference will firstly be made to Figures 1 to 4, which show a bag 1 constructed of polyolefin, preferably low density polyethylene, sealed hermetically along its entire periphery and having at one end a port 2 formed in one piece with and projecting from an elongate tapered body 3 from which there projects a further port

4. The ports 2 and 4 and the body 3 are constructed of the same material as the bag 1, the body 3 being incorporated into the peripheral bonding seam 5 of the bag 1 so that one end of the ports 2 and 4 opens inside the bag whereas their other end opens outside the bag.

As can be seen from Figure 2 the ports 2 and 4 define conduits closed by respective membranes 6 and 7 respectively, which are formed integrally with the ports and are arranged to ensure sterile conditions in the bag when it contains the product in powder form, as explained hereinafter.

From the figures it can also be seen that on the free ends of the two ports 2 and 4 there are applied protection plugs 8 and 9 respectively, which can be removed if required.

Before bonding the bag 1 along its entire periphery it is sterilized (for example with β rays), then into it, using an automatic machine in a sterile environment, there is fed a mass of sterile product in powder form 10 which, as can be seen from Figure 3, occupies only a small part of the bag capacity. The powder can be advantageously fed through that end of the bag distant from the end comprising the ports 2 and 4, after which this end is heat-bonded.

The described bag encloses and protects in a sterile environment the sterile product in powder form contained in it.

This bag can be easily and economically stored and transported to the user by the producer who has packaged it.

To make storage and transport very secure, the described bag 1 is preferably inserted into an intermediate bag 11 (Figure 5) also constructed of polyolefin, preferably high density polyethylene, and which after being sealed is inserted into an outer bag 12 composed of three layers of different materials welded together, of which the inner layer 13 is constructed of polyolefin

(preferably high density polyethylene) or polyvinyl chloride, the intermediate layer is constructed of a barrier material (preferably aluminium), and the outer layer is constructed of polyolefin, nylon or polyester.

The packaging of the bag 1 in the bags 11 and 12 is known, and is of the type illustrated in US-A-4,700,838, corresponding to EP-B-201880.

The nature of the barrier material in its general terms (additional to aluminium) can be as defined in US-A-4,910,147.

When the sterile product in powder form is to be used, the bag 1 is removed from the protection bags, the ~~/stopper/~~ plug 8 is unscrewed, and into the port 2 a perfuser is inserted so that its free end 16 fractures the membrane 6 (Figure 4). The perfuser is a well known device and will not be described for simplicity. Its end sealedly engages the cavity in the appendix 2, through which the desired quantity of water can be easily fed under sterile conditions into the bag 1 to form with the powdered product a solution 17 which fills only a part of the bag capacity. This merely partial filling of the bag 1, not only is necessary to enable the liquid in the bag to be energetically shaken in order to quickly and completely dissolve ~~/disperse or suspend/~~ the product in powder form to make it suitable for use, but it makes it possible to introduce into the bag the exactly controlled amount of liquid which is required for giving a solution in which the product is present at its predetermined concentration.
One of the preferred uses of the described bag is to preserve and transport sterile crystalline antibiotics and to form injectable solutions thereof (in hospitals and the like) in which the concentration of the antibiotics must be carefully controlled: this means that if the amount of an antibiotic closed in a bag is known, also the amount of water to be introduced into the same bag for forming the solution is known.
To give a detailed practical example, a bag 1 is prepared from a sheet of low density polyethylene of 150 micron thickness, the bag having a height of 35 cm and a width of 45 cm. 300 g of an antibiotic in powder form are fed into this bag and preserved in a sterile environment. The bag 1 is sealed within an intermediate bag of high density polyethylene of 100 micron thickness, having a height of 40 cm and a width of 48 cm. The intermediate bag is

then inserted into and sealed inside an outer bag of 43 cm height and 54.4 cm width formed from three layers joined together, the inner layer being formed of high density polyethylene of 0.075 mm thickness, the intermediate layer being formed of a sheet of aluminium of 0.01 mm thickness, and the outer layer being of polyester resin of 0.012 mm thickness.

When the antibiotic is to be used, the inner bag 1 is removed from the intermediate bag 11 and outer bag 12 and 3000 ml of injection-quality water are fed into it via the described perfuser (Figure 4) to form a solution of the required concentration for the particular therapeutic dose, in this case 100 mg/ml. It is important to note that the antibiotic solution 17 occupies only a part of the bag capacity to enable the antibiotic to be quickly and completely dissolved by vigorously shaking the bag. The bag capacity is preferably between 1.5 and 2 times the volume of the solution to be prepared in it.

The antibiotic solution obtained in this manner can be used directly, for example it can be transferred into sterile syringes each containing 30 ml of solution. The syringes can be filled in groups (for example 10, 20 or more syringes at a time) by automatic machines of known type which withdraw the solution through the free end 16 of the perfuser (by arranging the bag with the port 2 pointing downwards) used for feeding the liquid into the bag.

If desired, individual doses of the antibiotic solution can be withdrawn through the port 4 (the presence of which is not strictly necessary but is preferred). To do this, the ~~stopper~~ protection plug 9 is removed, and a rubber plug 20 (which seals that part of the cavity of the port 4 external to the bag 1) and the membrane 7 are perforated by the syringe needle.

When the syringe needle is removed, the solution is unable to flow from the bag 1, this being prevented by the rubber plug 20.

If the syringes are not used within a short time after their filling, they can be preserved in a freezer and then be despatched to the user in hospital in controlled temperature containers.

From the aforegoing description it is apparent that the antibiotic solution can be very easily and quickly formed at the desired concentration in a sterile environment, and that syringes can then be filled likewise easily and economically.

By proceeding in the aforedescribed manner, very important advantages are obtained compared with traditional systems in that it is no longer necessary to preserve the sterile antibiotic in powder form in glass bottles, a considerable reduction in the risk of contamination of the final pharmaceutical product is achieved (with the traditional system, for each syringe the solution has to be prepared individually and be fed into the syringe in environments which are generally not sterile), and there is a considerable cost and ecological saving consequent on the fact that it is no longer necessary to use glass bottles, metal rings, rubber plugs (one for each bottle), glass vials for solvents, etc.

All this leads to a considerable cost reduction, especially because a large number of specialized personnel are no longer required for preparing the individual antibiotic solutions, this being a very costly operation in hospitals or in those places in which a large quantity of antibiotic solutions has to be prepared.

Very considerable advantages are obtained even if the sterile products contained in the bags are not pharmaceutical products but are other products in powder form to be dissolved ~~/or dispersed/~~ in various liquids for their use, ~~/such as cell culture media./~~

In addition to the described bag, the invention also relates to the method for preserving and transporting sterile products in powder form and for dissolving ~~/or dispersing/~~ them in liquids under sterile conditions, as defined in the introductory part and in the claims accompanying this description.

ENCLOSURE 1

Claims:

1. A bag for preserving and transporting soluble sterile products in powder form and for forming therein solutions with predetermined concentrations of said products, the bag being of poyolefin construction, being hermetically sealed at its periphery to define a sterile closed space and having at least one port also of polyolefin construction defining a passageway the two ends of which open inside and respectively outside the bag, said passageway being closed by a pierceable membrane for the introduction of a solvent into the bag and respectively for the withdrawal of the solution therefrom, characterised in that each bag contains an amount of product in powder form adapt to give a solution with desired predetermined concentration, that such solution only partially fills the bag capacity, and in that the total volume of said solution is a multiple of single volumes of individual doses of the same solution.

2. A bag according to claim 1, characterized in that the amount of product in powder form enclosed within each bag is such that the bag capacity is between 1.5 and 2 the volume of the solution with predetermined concentration of such product.

3. A bag constructed of flexible polyolefin material and containing a ready to use solution prepared by

introducing within a sealed bag originally containing a dosed amount of a soluble sterile product in powder form an amount of solvent adapt to give said ready to use solution with desired concentration of said product, characterized in that the bag capacity is such that it is only partially filled by said ready to use solution, and in that the total volume of said solution is a multiple of single volumes of individual doses of the same solution.

4. A bag according to claim 3, characterized in that the bag capacity is between 1.5 and 2 times the volume of the solution formed therein.

5. A method for preparing solutions with predetermined concentrations of soluble sterile products in powder form enclosed and sealed within sterile bags constructed of flexible polyolefin materials, characterized in that a bag containing a dosed amount of soluble sterile product in powder form adapted to give a solution of predetermined concentration is fed with an amount of solvent adapt to give a ready to use solution with desired concentration of the product, in that the bag capacity is such that it is only partially filled by said solution, and in that the volume of the solution suffices to supply a plurality of single individual doses of the same solution.

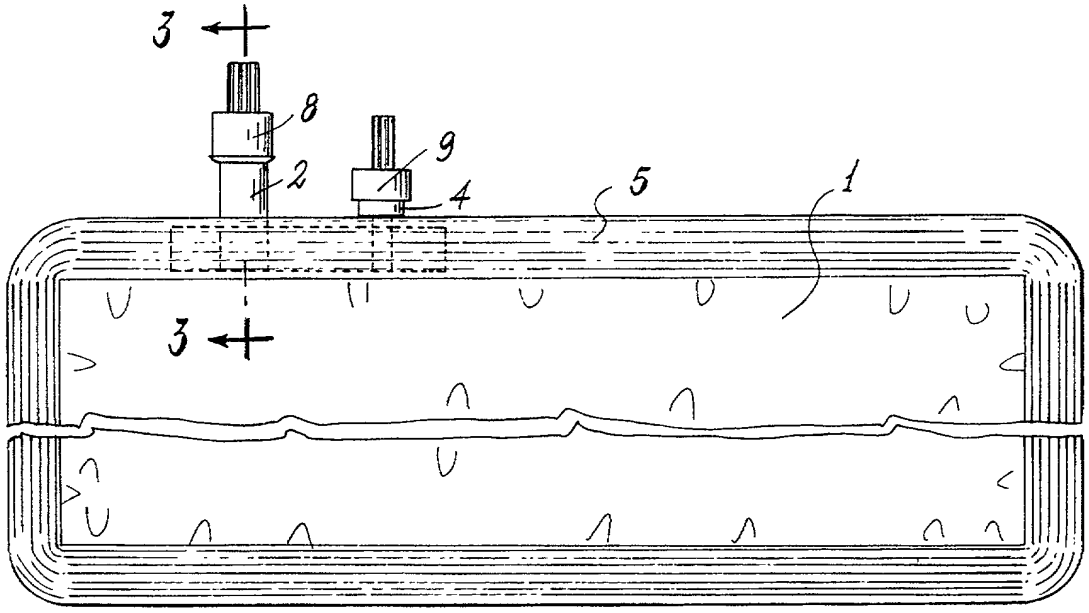

Fig. 1

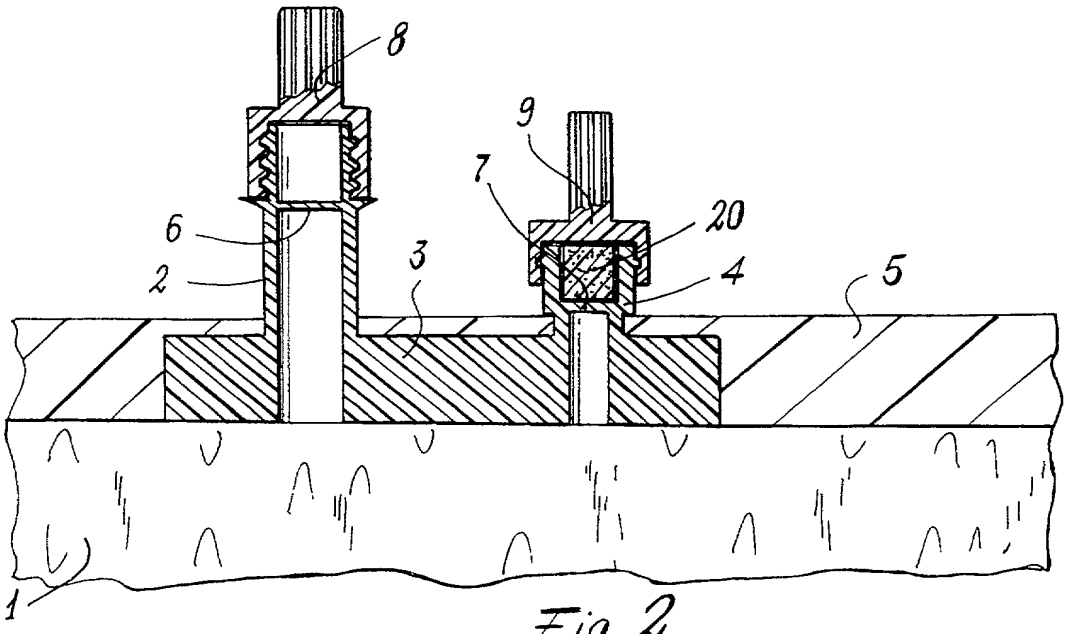

Fig. 2

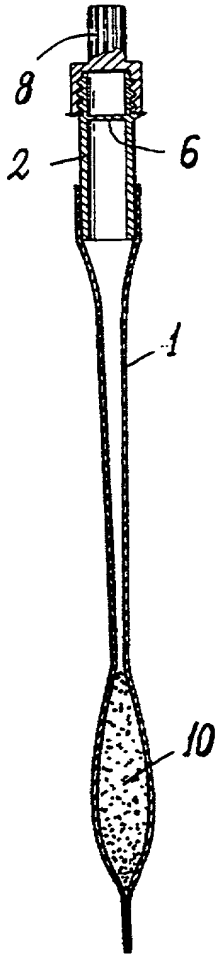

Fig. 3

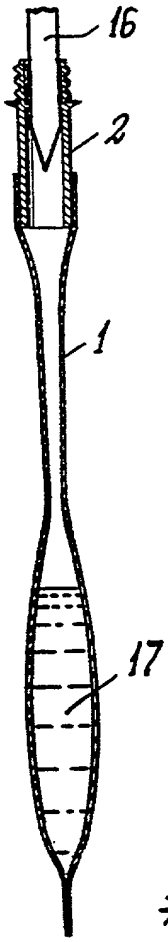

Fig. 4

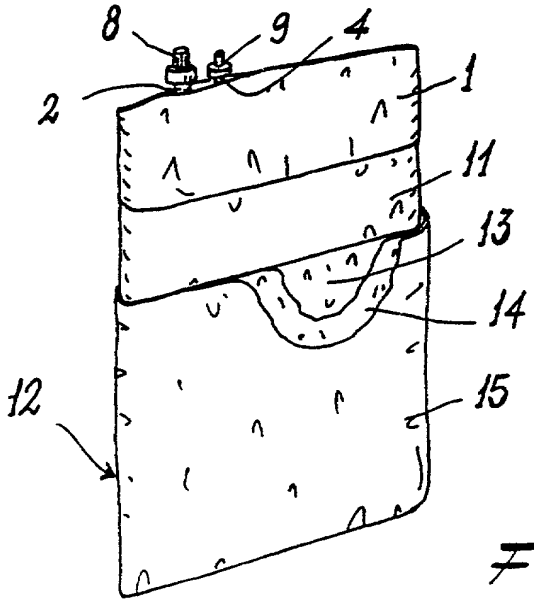

Fig. 5

USA

Declaration and Power of Attorney for Patent Application
Dichiarazione e procura ai fini della domanda di brevetto
Italian Language Declaration

Il sottoscritto inventore dichiara che:

La propria residenza, recapito postale e cittadinanza corrispondono a quanto indicato in calce, sotto la propria firma.

Ritiene di essere il primo ed unico inventore originale (se viene elencato in calce un solo nominativo) o il coinventore primo ed originale (se è elencato più di un nominativo) del oggetto rivendicato e per il quale il sottoscritto presenta domanda di brevetto. La invenzione in questione è chiamata.

_____

_____

_____

e la sua descrizione è allegata alla presente Dichiarazione a meno:

☐ è qui allegato

☐ Il _____

è stata depositata una domanda di brevetto statunitense numero o una domanda di brevetto internazionale PCT numero

_____ che è stata modificata il

_____ (se applicabile).

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled

BAG FOR PRESERVING AND TRANSPORTING STERILE PRODUCTS IN POWDER FORM AND FOR FORMING SOLUTIONS OF SAID PRODUCTS IN THE BAG

the specification of which:

☐ is attached hereto.

☐ was filed on _____

as United States Application Number or PCT International Application Number

_____ and was amended on

_____ (if applicable).

Il sottoscritto dichiara in oltre di aver letto e compreso il contenuto della descrizione identificata in precedenza, rivendicazioni comprese, come modificati dall'eventuale modifica summenzionata.

Il sottoscritto riconosce l' obbligo di rivelare informazioni essenziali ai fini della determinazione della brevettabilità ai sensi del Titolo 37, Codice dei Regolamenti Federali, § 1.56.

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above

I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations, § 1.56.

Italian Language Declaration

Il sottoscritto rivendica con la presente la priorità prevista dal Titolo 35, Codice degli Stati Uniti, § 119(e)-(d) o § 365(b) in relazione a qualsiasi domanda o domande estere di brevetto o certificato di inventore, o dal Titolo 35, § 365(a) degli stessi Codice in relazione a qualsiasi domanda internazionale PCT nella quale è designato almeno un paese diverso dagli Stati Uniti, i suddetti domande e certifcati essendo elencati sotto, e, spuntando les seguenti caselle, ha anche identificato sotto qualsiasi domanda estera di brevetto o certificato di inventore, o domanda internazionale PCT, la cui data di deposito preceda quella dalla domanda per la quale è rivendicata la priorità.

I hereby claim foreign priority under Title 35, United States Code, § 119(a)-(d) or § 365(b) of any foreign application(s) for patent or inventor's certificate, or § 365(a) of any PCT International application which designated at least one country other than the United States, listed below, and have also identified below, by checking the box, any foreign application for patent or inventor's certificate, or PCT International application having a filing date before that of the application on which priority is claimed.

Prior Foreign Application(s)
(Domande Estere Anteriori)

(Number) (Numero)	(Country) (Nazione)	(Day/Month/Year Filed) (Giorno/Mese/Anno di deposito)	Priority claimed Diritto di priorità rivendicato: Yes Sì	No No
MI98A0002256	Italy	20.10.1998	☒	☐
			☐	☐

Il sottoscritto rivendica con la presente i benefici previsti dal Titolo 35, Codici degli Stati Uniti, § 119(e), in relazione a qualsiasi domanda o domande provvisorie degli Stati Uniti elencate sotto.

I hereby claim the benefit under Title 35, United States Code, § 119(e) of any United States provisional application(s) listed below

(Application No.) (Nº della domanda)	(Filing Date) (Data di deposito)	(Application No.) (Nº della domanda)	(Filing Date) (Data di deposito)

Il sottoscritto rivendica con la presente i benefici previsti dal Titolo 35, Codice degli Stati Uniti, § 120, in relazione a qualsiasi domanda o domande statunitensi, o dal Titolo 35, § 365(c) degli stessi Codice in relazione a qualsiasi domanda internazionale PCT nella quale sono designati gli Stati Uniti, i suddette domande essendo elencate sotto e, nella misura in cui l'oggetto di ciascuna rivendicazione di questa domanda non sia stato esposto nella domanda statunitense o internazionale PCT anteriore nel modo previsto dal primo paragrafo del Titolo 35, Codice degli Stati Uniti, § 112, riconosce l'obbligo di rivelare informazioni essenziali ai fini della determinazione della brevettabilità ai sensi del Titolo 37, Codici dei Regolamenti Federali, § 1.56, le quali diventino disponibili durante il periodo compreso tra la data di deposito della domanda anteriore e la data di deposito nazionale o internazionale PCT della presente domanda.

I hereby claim the benefit under Title 35, United States Code, § 120 of any United States application(s), or § 365(c) of any PCT International application designating the United States, listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT International application in the manner provided by the first paragraph of Title 35, United States Code, § 112, I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations, § 1.56 which became available between the filing date of the prior application and the national or PCT International filing date of this application.

(Application No.) (Nº della domanda)	(Filing Date) (Data di deposito)	(Status) (patented, pending, abandoned) (Stato) (concessione di brevetto, in corso di esame, abbandono)
PCT/EP99/02745	23 April 1999	pending

Con la presente, il sottoscritto dichiara veritiere tutte le affermazioni contenute in questa domanda in relazione alle proprie conoscenze e di ritenere vere tutte le affermazioni o informazioni presentate. Dichiara inoltre che tali asserzioni sono state espresse nella piena consapevolezza che le dichiarazioni intenzionalmente false sono punibili con una poulte, l' incarcerazione o entrambe, ai sensi della Sezione 1001 del Titolo 18 del Codice degli Stati Uniti e che tali dichiarazioni entenzionalmente false possono mettere a repenfaglio la validità della domanda o di qualsiasi brevetto ruasciato in merito

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Italian Language Declaration

PROCURA: Il sootscritto inventore nomina con la presente il seguente avvocato o avvocati e/o agente o agenti al fine di istruire questa pratica e di condurre tutte le operazione ad essa pertinenti presso l'Ufficio dei Brevetti e Marchi di Fabbrica: (Elencare il nome ed il numero di matricola).

POWER OF ATTORNEY: As a named inventor, I hereby appoint the following attorney(s) and/or agent(s) to prosecute this application and transact all business in the Patent and Trademark Office connected therewith: *(list name and registration number)*

Norman F. Oblon, Reg. No. 24,618; Marvin J. Spivak, Reg. No. 24,913; C. Irvin McClelland, Reg. No. 21,124; Gregory J. Maier, Reg. No. 25,599; Arthur I. Neustadt, Reg. No. 24,854; Richard D. Kelly, Reg. No. 27,757; James D. Hamilton, Reg. No. 28,421; Eckhard H. Kuesters, Reg. No. 28,870; Robert T. Pous, Reg. No. 29,099; Charles L. Gholz, Reg. No. 26,395; William E. Beaumont, Reg. No. 30,996; Jean-Paul Lavalleye, Reg. No. 31,451; Stephen G. Baxter, Reg. No. 32,884; Richard L. Treanor, Reg. No. 36,379; Steven P. Weihrouch, Reg. No. 32,829; John T. Goolkasian, Reg. No. 26,142; Richard L. Chinn, Reg. No. 34,305; Steven E. Lipman, Reg. No. 30,011; Carl E. Schlier, Reg. No. 34,426; James J. Kulbaski, Reg. No. 34,648; Richard A. Neifeld, Reg. No. 35,299; J. Derek Mason, Reg. No. 35,270; Surinder Sachar, Reg. No. 34,423; Christina M. Gadiano, Reg. No. 37,628; Jeffrey B. McIntyre, Reg. No. 36,867; William T. Enos, Reg. No. 33,128; Michael E. McCabe, Jr., Reg. No. 37,182; Bradley D. Lytle, Reg. No. 40,073; and Michael R. Casey, Reg. No. 40,294, with full powers of substitution and revocation.

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Nome e cognome dell'unico o del primo inventore Marco FALCIANI	Full name of sole or first inventor Marco FALCIANI
Firma dell'inventore Data	Inventor's signature Date 01 Febr.2001
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Cittadinanza	Citizenship Italian
Recapito postale	Post Office Address same as above
Nome e cognome dell'eventuale secondo coinventore Sergio DUSCI	Full name of second joint inventor, if any
Firma del secondo coinventore Data	Second Inventor's signature Date 01 Febr.2001
Residenza	Residence Via Roma, 25 - 23020 TRESIVIO (SO) - IT
Cittadinanza	Citizenship Italian
Recapito postale	Post Office Address same as above

(Fornire le stesse informazioni e le firme del terzo e degli ulteriori coinventori.)

(Supply similar information and signature for third and subsequent joint inventors

1/00